REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claims 21 and 22 have been revised to define the invention with additional clarity and new claim 28 has been added. The claims as presented are fully supported by an enabling disclosure. In this regard, attention is directed to the fact that the use of activin to reduce scarring associated with wound healing is clearly contemplated throughout the specification, and is the subject of the experimental results reported.

Claims 20-22 and 24-27 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is in order for the reasons that follow.

In rejecting the claims as lacking written description, the Examiner appears to contend that each and every stimulator of activin must be structurally defined. No basis is seen for such a requirement. The disclosure is replete with examples of activin stimulators defined structurally, functionally or both. In view of the description provided, it would have been clear that Applicant was in possession of the entirety of the claimed invention at the time of filing.

Reconsideration is requested.

Claims 20-22, 24 and 25 stand rejected under 35 USC 102(e) as allegedly being anticipated by Mitrani. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

It was a new and non-obvious finding on the part of Applicant that activin can be used to promote healing with reduced scarring. The effects of activin on scarring are dose dependent. That is, different doses have markedly different effects on scarring. The doses described in the present specification all have beneficial effects on scarring (when assessed either

macroscopically or microscopically). The doses considered by Mitrani are far higher than those shown by Applicant to promote healing with reduced scarring. Instead, the doses suggested by Mitrani would actually increase scarring.

Mitrani suggests that activin should be used in a dose range of between 0.001mg/kg and 50mg/kg body weight. Preferred dose ranges of activin are stated to be between 0.01mg/kg and 10mg/kg body weight.

The studies described in the instant application utilized rats weighing between 200g and 250g. These were treated with one of three separate regimes:

i) three administrations, each of 2.5ng;

ii) three administrations, each of 5ng; or

iii) three administrations, each of 10ng.

Thus, in the lowest dosing regime, a total of 7.5ng of activin was administered per rat, and in the highest dosing regime, a total of 30ng of activin was administered per rat. These totals, respectively, correspond to between 34.1 and 30ng/kg body weight (depending on size of rat) and between 136.4 and 120ng/kg body weight.

It can readily be seen that these doses are considerably lower than those suggested in Mitrani. The lowest dose considered by Mitrani corresponds to 1μg/kg, and the lowest preferred dose to 10μg/kg. In contrast, the highest dose shown by Applicant to reduce scarring is 0.136μg/kg (about one eighth of the lowest suggested by Mitrani), and the lowest dose is only 0.03μg/kg (just 3% of the lowest dose suggested by Mitrani). Clearly, the skilled person following the teachings of Mitrani would not have arrived at a scar-reducing dose of activin, as required by the instant invention.

Furthermore, doses in the range of those suggested by Mitrani have been shown to be pro-scarring, rather than anti-scarring.

By way of example, transgenic mice that over-express activin A in the basal epidermis (calculated to lead to between 20 and 150ng activin/ml blood – Munz et al 1999) exhibit enhanced scarring in response to full thickness excisional wounds (unpublished data from Munz et al, and described in Wankell et al 2003, and Sulyok et al 2004).

Rats of 200 to 250g weight have an average blood volume of approximately 13.5mls. Thus, rats treated with regime (iii) above can be expected to achieve a total accumulation of 2.22ng activin/ml blood (based on administration of a total of activin 30ng activin, and assuming no breakdown of activin). This figure (for the highest dose regime contemplated by Applicant) is approximately one tenth of the lowest value reported by Munz et al in mice exhibiting increased scarring. In turn, the lowest concentration of activin reported by Munz et al (approximately ten times that established by regime (iii)) is generally comparable with that arising from the lowest dose considered by Mitrani (approximately eight times that established by regime (iii)).

In the light of the above, it can be seen that an artisan, following the teachings of Mitrani, would not have arrived at the subject matter of the present claims (e.g., use of activin in an amount sufficient to reduce scarring) but would, in fact, have been led to use amounts of activin that would increase scarring.

In view of the above, reconsideration is requested.

Claims 20-22, 24 and 25 stand rejected under 35 USC 102(b) as allegedly being anticipated by De Kretser. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and for the reasons that follow.

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The disclosure of De Kretser et al is entirely silent as to doses of activin that are to be used. Given the lack of this teaching, and the dose dependency discussed above, De Kretser et al cannot be viewed as being inherently anticipatory. Accordingly, reconsideration is requested.

Claims 20, 21, 26 and 27 stand rejected under 35 USC 103 as allegedly being obvious over Mitrani in view of Ferguson. These same claims stand rejected as obvious over De Kretser et al in view of Ferguson. The rejections are traversed for the reasons that follow.

The fundamental failings of Mitrani and De Kretser are detailed above. Nothing in Ferguson would have cured the deficiencies of the primary references. Further, the Examiner is reminded that subject matter that is allegedly inherent cannot be relied upon in rejecting claims as obviousness. Reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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